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Post-gonococcal cervicitis and post-gonococcal urethritis

A study of their epidemiological correlation and the role of Chlamydia trachomatis in their aetiology

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SUMMARY In a study of 157 men and 141 women with gonorrhoea post-gonococcal urethritis (PGU) in men was significantly more common among chlamydia-positive (76%) than among chlamydia-negative (22·5%) patients. Clinical investigations of PGU detected 95% of the patients infected with *C trachomatis*. PGU was, however, asymptomatic in over half of the patients and a careful follow-up for 3-6 weeks was necessary to detect between 80% and over 90% of cases. PGU was not related to age, past history of gonorrhoea or non-gonococcal urethritis, severity of gonococcal infection, or chlamydial inclusion count.

Although post-gonococcal cervicitis (PGC) in women was an identifiable entity, it was detected in only one-third of chlamydia-positive patients. PGC was significantly associated with the 20-29 year-old age group but was not related to symptoms or chlamydial inclusion count. In the absence of facilities for culturing chlamydia, selection on an epidemiological basis of all female consorts of men with PGU, together with the remaining women with PGC, would have resulted in some unnecessary treatments and left untreated up to 30% of those harbouring *C trachomatis*.

Introduction

Post-gonococcal urethritis (PGU)—that is, urethritis persisting or developing in men after treatment of gonorrhoea with penicillin or spectinomycin—is now well recognised. Willcox[1] recently discussed the epidemiological importance of concealed non-gonococcal urethritis (NGU) in men with gonorrhoea. Almost half of these men will be found to have PGU after treatment with penicillin.[2] *Chlamydia trachomatis* has been isolated from about 50% of these men.[3]

A diagnosis of PGU is easily made when an excess of polymorphonuclear leucocytes is seen on microscopy of smears of urethral secretions or urine threads or the centrifuged sediment of first-voided urine. No such criterion exists for the diagnosis of non-gonococcal or post-gonococcal cervicitis (PGC). The endocervix normally contains clear or cloudy mucus, in which the number of leucocytes varies with the menstrual state and possibly other factors. Macroscopic cervicitis, however, comprising oedematous and congested ectopy (hypertrophic "erosion") and mucopus in the endocervix (singly or in combination), has been found to be significantly associated with infection due to *C trachomatis*.[4-7] Rees[8] described persistence of cervicitis in cases of combined gonococcal and chlamydial infection after treatment with penicillin. Conversely, a single layer of columnar epithelium overlying the stromal capillary bed and hence appearing red (which may be termed "simple" ectopy, flush with the surrounding cervix) is not a pathological entity.[9 10]

We decided to observe carefully the macroscopic changes in the cervix and to compare those patients infected with *C trachomatis* as well as *Neisseria gonorrhoeae* (combined infection) with those

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infected with *N gonorrhoeae* alone before and after treatment with penicillin or spectinomycin, neither of which is expected to be effective against *C trachomatis*. The other aim of this study was to define additional correlates which may have predictive value for PGU in male and PGC in female patients.

Patients and methods

New patients seen on Mondays and Thursdays between 1976 and 1978 were included in the study, provided they had not had a sexually transmitted disease in the preceding three months nor received a sulphonamide or an antibiotic in the preceding month.

Demographic data, past history, history of recent sexual exposure, and symptoms and signs were recorded on precoded proformas.

DIAGNOSIS

Men

Urethral specimens were collected for smears for Gram staining and for cultures for *N gonorrhoeae* and *C trachomatis*. Swabs made of sterile plain cottonwool on a thin metal wire (Medical Wire and Equipment Co Ltd) were inserted between 3 and 5 cm into the urethra, rotated several times, and withdrawn; two of these were then broken into the respective transport media before being cultured.

Women

Specimens were collected from the urethra for culture of *N gonorrhoeae* and from the endocervix for culture of *N gonorrhoeae* and *C trachomatis*. Culture methods for both organisms have been described.[7]

Chlamydial inclusion count

Urethral and cervical smears were graded "low" or "high" (positive) according to the number (<120 or ⩾120 respectively) of *C trachomatis* inclusions found on inoculated coverslips.

TREATMENT OF GONORRHOEA AND FOLLOW-UP

Gonorrhoea was treated with either procaine penicillin 1·2 megaunits intramuscularly plus probenecid 1 g orally or spectinomycin 2 g intramuscularly.

Patients were advised to abstain from sexual intercourse until they and their partners were cleared of infection and to return weekly for three weeks and then at increasing intervals; male patients were asked not to pass urine for at least three hours before each visit. At each visit the patient was interviewed about further sexual exposure, interim medication, and symptoms, and repeat specimens were collected for microscopy and culture of *C trachomatis* and *N gonorrhoeae*.

Post-gonococcal urethritis

PGU in men was diagnosed if urethral smears and cultures showed no evidence of gonococcal infection and if the urethral secretion or urine threads showed >15 polymorphonuclear leucocytes in >5 high power fields (× 100 objective, × 6·3 binocular eyepiece). To exclude the possibility of resolving urethritis, PGU was diagnosed after one week's follow up only if urethral discharge was present.

Post-gonococcal cervicitis

PGC was diagnosed if urethral and endocervical smears and cultures showed no evidence of gonococcal infection and if there was mucopus in the endocervix or hypertrophic ectopy and a congested cervix.

STATISTICAL ANALYSIS

The data were analysed with a computer using the "Statistical Package for the Social Sciences". Tests for significance were performed using the χ^2 statistic with Yates's correction.

Results

POST-GONOCOCCAL URETHRITIS

Diagnosis

Gonorrhoea was diagnosed in 157 of the male patients with urethritis. Of these, 65 (41·4%) also harboured *C trachomatis* (55 infections were detected on the first and 10 on the second set of investigations). After excluding those who defaulted or had had further sexual contact, 121 of the 145 men with gonorrhoea treated with penicillin or spectinomycin were eligible for re-evaluation.

PGU developed in 38 (76%) of the 50 men who were chlamydia-positive but in only 16 (22·5%) of the 71 who were chlamydia-negative (highly significant difference: $\chi^2_1 = 31·81$, $P<0·001$). The incidence of PGU was similar whether gonorrhoea was treated with penicillin (25/58, 43%) or spectinomycin (29/63, 46%). Of the 12 who were initially chlamydia-positive but did not develop PGU, six became and remained chlamydia-negative during observation for 12 weeks; three defaulted after one, two, and six weeks while their investigations still gave positive results for chlamydia. Cultures for chlamydia were not repeated in the remaining three cases.

Chlamydial inclusion count

An initial chlamydial inclusion count was available

for 34 patients. The incidence of PGU was higher among those with high counts (15/18, 83%) than among those with low counts (11/16, 69%), but the difference was not significant ($\chi^2_1 = 0{\cdot}35$, $P > 0{\cdot}5$).

Epidemiological data

Age, marital state, past history of gonorrhoea and NGU, last exposure and number of partners, severity of symptoms (urethral discharge or dysuria or both), duration and quality of discharge (mucoid or purulent) were not significantly associated with the development of PGU.

Duration of follow up

PGU was detected in 28 (52%) of the 54 patients in the first two weeks after treatment for gonorrhoea, in 43 (80%) within three weeks, and in all but four (93%) within six weeks. The time of detection of PGU was not influenced by the choice of treatment with either penicillin or spectinomycin.

Symptoms and signs

Of the 54 patients with PGU, 29 (54%) had no symptoms one week after treatment for gonorrhoea and up to the time their PGU was detected (only four of these had been asymptomatic initially); 18 complained of recurrence of, or persistent but less profuse, urethral discharge mainly in the mornings; one, who was asymptomatic initially, had noticed the discharge for the first time after treatment; four had urinary symptoms only; and two had discharge plus dysuria. Urethral discharge, mostly scanty and mucoid, was present (usually only on stripping) in 32 patients, although only 21 complained of it.

POST-GONOCOCCAL CERVICITIS

One hundred and forty-one women with gonorrhoea were treated with penicillin or spectinomycin; 115 (50 chlamydia-positive, including three chlamydia-negative on the first but positive on the second set of investigations, and 65 chlamydia-negative) were eligible for assessment for PGC. After treatment, 13 of the 50 chlamydia-positive patients subsequently became and remained chlamydia-negative up to their last follow-up visit, which was at 2-3 weeks for four, six weeks for one, 12 weeks for three, and six months or longer for five. Thirty-seven patients remained chlamydia-positive up to the time their chlamydial infection was treated, which was at 1-2 weeks for five, 3-6 weeks for 21, 7-12 weeks for six, and over 12 weeks for five (six months in one case).

Signs

Among those found at initial examination to have simple or no ectopy and clear or mucoid discharge, the condition of the cervix and contents remained the same after treatment in 95%, whether chlamydia-positive (23/24) or chlamydia-negative (41/43). In 48 patients, however, whose initial examination showed macroscopic cervicitis, the appearance of the cervix or its contents had not improved in 16 (62%) of the 26 chlamydia-positive compared with six (27%) of the 22 chlamydia-negative patients; the difference was significant ($\chi^2_1 = 4{\cdot}34$, $P < 0{\cdot}05$).

Treatment

After treatment of the chlamydial infection with oxytetracycline, erythromycin, or sulfametopyrazine (Arya *et al*, unpublished data) congestion and oedema of the cervix and endocervical mucopurulent discharge resolved in all except two patients. One of the latter, who remained chlamydia-positive, admitted to further exposure with the same but yet untreated partner; the other had been treated with a single dose of sulfametopyrazine 2 g but had remained repeatedly chlamydia-negative for over six months.

Chlamydial inclusion count

An initial chlamydial inclusion count was available for 36 patients. PGC was present in five of the 19 patients with low counts and in nine of the 17 with high counts; the difference was not significant ($\chi^2_1 = 1{\cdot}67$, $P > 0{\cdot}1$).

Age

PGC was more common among those patients aged 20-29 years (20/62, 32%) compared with those aged 15-19 years (2/33, 6%) and those aged 30 or more (3/20, 15%) whether they harboured chlamydia or not. The difference between age groups 20-29 years and 15-19 years was significant ($\chi^2_1 = 6{\cdot}89$, $P < 0{\cdot}01$).

Symptoms

Concomitant infections such as candidosis and trichomoniasis, which may contribute to symptoms,[7] had been treated with appropriate regimens by the time the patients were reassessed. Whereas vaginal discharge was almost equally common before treatment for gonorrhoea among those with cervicitis, whether or not they harboured chlamydia (14/26, 54%, and 11/22, 50% respectively), a higher proportion (6/17, 35%) with cervicitis and harbouring chlamydia had vaginal discharge after treatment compared with those not harbouring chlamydia (1/8, 12%). This difference was not significant.

PGC IN RELATION TO PGU IN MALE PARTNERS

Male partners of 95 women were seen at the same clinic; 89 of the former had gonorrhoea (the presence or absence of PGU was unknown for nine) and six NGU. The number of men and women harbouring

chlamydia is shown in the table. Although the numbers in each category are small, PGU in men was associated with PGC in women—that is, female consorts of 13 (33%) of the 40 men with PGU had PGC compared with those of six (15%) of the 40 men who did not develop PGU ($\chi^2_1 = 2 \cdot 48$, $P > 0 \cdot 1$).

Discussion

Although PGU in men is an established clinical entity, a careful examination is necessary to exclude or confirm its presence after treatment of gonorrhoea with penicillin or spectinomycin. Concomitantly acquired *C trachomatis* infection, found in 41·4% of the patients in this study, is a common cause of PGU. The proportion (54%) of patients with PGU who were asymptomatic was probably high because the quick resolution of the usually severe symptoms associated with gonorrhoea had obscured any mild residual symptoms. This explanation is supported by the fact that a urethral discharge was present—albeit usually only on stripping—in 32 patients, although only 21 complained of it. Most of the patients had followed the advice of holding their urine for at least three hours before attending the clinic. Pyuria was thus evident in all cases diagnosed. In the absence of facilities for culturing *C trachomatis*, however, three chlamydia-positive patients without symptoms or signs of urethritis would have been missed, one of whom remained chlamydia-positive for at least six weeks after treatment for gonorrhoea. On the other hand, six patients who were initially chlamydia-positive became and remained chlamydia-negative after treatment and did not develop symptoms and signs of urethritis, thus being "spontaneously" cured up to the observation period of 12 weeks.

The development of PGU was not influenced by age, past history of gonorrhoea or NGU, the severity of the gonococcal infection, or the chlamydial inclusion count. When gonorrhoea was treated with penicillin or spectinomycin, a follow up of at least three weeks was necessary to detect 80%, or six weeks to detect 93%, of cases of PGU.

Although *C trachomatis* does not cause cervical ectopy, the latter's presence does increase susceptibility to chlamydial infection.[7] In a proportion of cases the ectopic cervix becomes oedematous or hypertrophic[4 7] with or without mucopurulent discharge in the endocervix. We observed that the appearance of cervicitis persisted in 62% of the patients with a combined infection (gonococcal and chlamydial) after treatment of gonorrhoea with penicillin or spectinomycin, which thus suggests that PGC is an identifiable entity. Resolution of these manifestations (that is, hypertrophic ectopy becoming simple and mucopurulent discharge becoming clear or mucoid) after treatment of the chlamydial infection with an appropriate antibiotic provided further proof (unpublished data).

TABLE *Relationship between post-gonococcal urethritis (PGU) in male partners and post-gonococcal cervicitis (PGC) in women*

	PGC in 50 women chlamydia-positive before treatment for gonorrhoea						*PGC in 65 women chlamydia-negative before and after treatment for gonorrhoea*			
	*After treatment**									
	Chlamydia-positive			*Chlamydia-negative*						
Male partner	*PGC+*	*PGC−*	*Total*	*PGC+*	*PGC−*	*Total*	*PGC+*	*PGC−*	*Total*	*Grand total*
Chlamydia +										
PGU +	6	11	17	0	1	1	1	5	6	24
PGU −		1	1							1
PGU?										
Chlamydia −										
PGU +		1	1					2	2	3
PGU −	1	2	3		1	1	4	8	12	16
PGU?								1	1	1
No chlamydial culture										
PGU +	4	1	5	2	2	4		4	4	13
PGU −		1	1	1	2	3	1	18	19	23
PGU?	1	2	3		2	2	1	2	3	8
Non-gonococcal urethritis										
Chlamydia +	1	1	2							2
Chlamydia −								1	1	1
Chlamydia (ND)		1	1				1	1	2	3
Not seen	1	2	3		2	2		15	15	20
Total	14	23	37	3	10	13	8	57	65	115

+ Present; − absent; ND = not done; ? = unknown
*For gonorrhoea

As in men, a proportion of women with combined infection became and remained chlamydia-negative after treatment of gonorrhoea, five remaining so for at least six months. Similarly, of the 37 who were persistently chlamydia-positive, five remained so for over 12 weeks (one for six months) without apparently developing any complications. Studies of cervical cytology in such cases would be of interest in view of the reported association between chlamydial infection and cervical intraepithelial neoplasia.[11] PGC was found to be more common among those aged 20-29 years but was not related to symptoms or the initial chlamydial inclusion count.

It may be assumed that the recognition of PGU in men would lead to identification of most of the cases (95% in this study) who needed treatment because of a concomitant chlamydial infection. If identified, however, PGC would account for only one-third of those who were chlamydia-positive—that is, 17/50 in this study (or 14/37 after excluding those who became chlamydia-negative) (table). If, as has been suggested,[1] all of the 115 women were to be treated with a regimen effective against both chlamydia and gonorrhoea, then at least 26 (23%) women who were chlamydia-negative and did not have PGC and whose male partners did not develop PGU would be unnecessarily treated, together with possibly some of the 15 women who were chlamydia-negative, did not develop PGC, and whose male partners were not seen (table).

Another approach, in the absence of facilities for culturing *C trachomatis,* would be to treat all women whose male consorts developed PGU or NGU as well as any with evidence of macroscopic PGC. If the female consorts of all 46 men with PGU or NGU seen in this study were treated using these criteria, 31 initially chlamydia-positive women (including 18 with no PGC) would be treated; if all the remaining women with PGC were also treated, three more chlamydia-positive women would be covered at the cost of another nine treatments. By so doing, however, 15 chlamydia-positive cases would be missed, although seven of these had become chlamydia-negative after treatment for gonorrhoea.

Clearly, neither of the above methods provides a satisfactory solution; this can only be achieved by the provision of an appropriate service for culturing *C trachomatis,* especially for women. This facility will also enable us to uphold the fundamental principle of "diagnosis before treatment".

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